AMENDMENTS TO THE SPECIFICATION

Please amend the title as follows:

~~MOLECULAR MODELING METHODS~~

METHOD OF MODELING COMPLEX FORMATION BETWEEN A QUERY LIGAN AND A TARGET MOLECULE

Please replace the paragraph beginning at page 27, line 9 with the following amended paragraph:

All software was written at Vertex Pharmaceuticals, Inc. in Python, Perl or C++ unless otherwise noted. Routines that require molecular representation use the Python or C++ interface to the OEChem library (OpenEye Scientific Software, Santa Fe, NM 87507). **X-ray Structures**. FASTA (Pearson, W.R., Lipman, D.J. *PNAS*. 1988, 85 2444-2448) was used to identify X-ray structures in the protein data bank (pdb)(Berman, H.M., et al., *Nucleic Acids Research*. 2000, 28, 235-242) with sequences homologous to the kinase domain of pkaα using a cutoff value of 3. Because a high cutoff value was used, the choice of reference kinase sequence does not affect the results. Only structures containing a ligand that binds to the ATP pocket of the kinase were included in the analysis. For pdb files containing multiple structures of the same kinase domain with different chain names, only the first chain containing the kinase domain was included in the analysis. The X-ray structures were aligned in a common coordinate frame by superimposing backbone atoms (N, CA and C) of residues corresponding to 142 – 149 in thejnk3 hinge region onto the jnk3 reference structure (pdb code 1jnk; Xie, X., et al., Structure. 1998, 6, 983-991) using the McLachlan algorithm (McLachlan, A.D., *Acta Cryst* 1982, A38,871-873) as implemented in the program ProFit (Martin, A.C.R, ~~http://www.bioinf.org.uk/software/profit~~. bioinf.org.us/software/profit.)

Please replace the paragraph beginning at page 27, line 25 with the following amended paragraph:

Separate files for ligand and protein atoms were extracted from each aligned pdb file. A SMILES string was obtained for each ligand by converting the IUPAC name in the HETNAM

record of the pdb file to SMILES using Chemdraw™ (CambridgeSoft, Cambridge, MA 02140) with manual error checking. The SMILES string and pdb coordinates were then used to create an MDL mol file (MDL Information Systems, San Leandro, CA 94577). A framework library was created by reducing the molecules to frameworks using the method described by Bemis and Murcko (*J Med Chem* 1996, *39*, 2887-2893), except that molecular framework carbonyl oxygen atoms directly connected to framework atoms were included.

Please add the following paragraph to the top of page 35:

Table 1, cont.

Please add the following paragraph to the top of page 36:

Table 1, cont.

Please add the following paragraph to the top of page 37:

Table 1, cont.

Please add the following paragraph to the top of page 38:

Table 1, cont.

Please add the following paragraph to the top of page 39:

Table 1, cont.

Please add the following paragraph to the top of page 40:

Table 1, cont.

Please add the following paragraph to the top of page 41:

Table 1, cont.

Please add the following paragraph to the top of page 42:

Table 1, cont.